Extracted from the American Journal of the Medical Sciences for July, 1881.

MAY IODIDE OF POTASSIUM EXCITE BRIGHT'S DISEASE?

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MAY IODIDE OF POTASSIUM EXCITE BRIGHT'S DISEASE?[1]

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WHERE there is afforded opportunity of examining after death, the bodies of persons who have suffered from late syphilis, an astonishingly large number of them will be found to present evidences of disease of the kidneys. In 24 autopsies of syphilitic subjects, Lancereaux observed renal degenerative changes 8 times (*Gaz. Hebd.* 1, 1864, p. 502). Moxon detected alterations in these organs in 14 out of 25 post-mortem examinations of syphilitics at Guy's Hospital (*Guy's Hosp. Reports*, 1868, p. 329). It must be acknowledged, however, that if we consider the whole number of persons who have had syphilis, the proportion who develop kidney disease is exceedingly small. Indeed, with very few exceptions, syphilis and kidney disease would seem to exist in the relations of cause and effect only among those unfortunates who experience the late or tertiary manifestations of the affection.

Pathologists have long been aware that the diseased kidneys of syphilitic persons present differences as great in microscopic as in gross appearances, changes that may be encountered with equal, even with greater frequency, as results of other affections, as well as changes that are essentially syphilitic. Of the forms of disease to which I now refer, the most frequent by far is one that is not in itself syphilitic. This is lardaceous or albuminoid degeneration, and was first described as of syphilitic origin, by Rayer, in 1840 (*Maladies des Reins*, t. ii. p. 489). All subsequent writers have remarked its frequency. Moxon, in the article already quoted, observed, in his 27 autopsies, lardaceous degeneration of the kidneys 11 times. But the frequency of lardaceous disease as the result of syphilis, may be more readily appreciated by studying the etiology of this form of degeneration. Thus Fehr (quoted by Roberts) reported syphilis as present in 34 out of 145 cases of lardaceous kidney. Dickinson (*Dis.*

[1] Read at the meeting of the American Medical Association, at Richmond, May 4, 1881.

of Kidneys, part ii. 1877, p. 473), compiled 83 cases of lardaceous disease from the dead-house reports of St. George's Hospital, the presence of syphilis being noted 18 times. This form, when of syphilitic origin, is identical with the same degeneration in persons free from the disease. It is true that some writers, Beer more especially (*Die Eingeweide Syphilis*, 1867), describe peculiar conditions and distributions of the process, to be met with only in syphilitics; but these lack confirmation. On the other hand, there is a form of renal disease quite characteristic of syphilis, the circumscribed, new formation known as gummy tumour. This is of exceedingly rare occurrence. Moxon found it but once in his 27 autopsies, where there were 16 cases of renal disease. In Lancereaux's 24 autopsies, where kidney disease was detected 8 times, gummy tumours were met but once. Numerous cases of gumma of the kidney have been recorded, but the lesion is undoubtedly a rare one. From 1 to 20 may be encountered, and their size may vary from a mere point to the dimensions of "a small potato." It is stated, upon the authority of Beer, Moxon, and others, that purely parenchymatous nephritis may be dependent upon syphilis. It must be very infrequent. But there is still another form of renal alteration of syphilitic origin.

Generally diffused, interstitial hyperplasia and subsequent fibrosis of the kidneys, not associated with lardaceous disease, is rare in syphilitics; and yet it is not uncommon to find these organs with circumscribed areas of interstitial hyperplasia, or of its cicatricial remains, distinct from ordinary gummy tumor. Just as one finds in other organs, notably, the liver, lungs, and testicle, syphilitic inflammation, not at all differing in their appreciable morbid appearances from simple inflammations, so, in the kidneys, we encounter diffused interstitial nephritis, that except for a disposition to more circumscribed distribution is like interstitial nephritis from other causes.

Where the process involves the entire organ, there is no way of deciding upon its specific origin. Most frequently, however, only a portion of the kidney is affected, and when considerable contraction has resulted from this form of interstitial disorder, it is often seamed with scars, which from their circumscribed arrangement, are very characteristic. It is not unlikely that localized cicatrices may sometimes result from the absorption of gummy tumours. A considerable degree of fatty degeneration of the epithelia of the tubules often accompanies these processes.

From the foregoing remarks, it will be seen that of the different alterations to which the kidneys of syphilitics are liable, but one can be regarded as certainly syphilitic, the gummy tumour, the most rare of all. Diffused nephritis can only be recognized as *probably* syphilitic, when of limited and circumscribed extent. On the other hand, lardaceous degeneration, most often observed, is only a result of syphilis as it is a result of tubercle, of scrofula, of prolonged suppuration. Now, while it is certain

that we may have these forms of disease due to syphilis, it by no means follows that disease of the kidneys in syphilitics is always of syphilitic origin. May it not arise from adventitious causes more often than is generally supposed?

It is evident, that apart from any influence that syphilis may exert in renal pathology, the kidneys of syphilitics are just as subject to morbific influences as those of healthy people, and that one should not necessarily attribute to this disease lesions that are not characteristically specific.

One occasionally finds in medical literature, statements that albuminuria and nephritic inflammation have been known to arise in consequence of the ingestion of the iodide of potassium. These reports, it is true, are few in number and quite vague in character, and yet they come from sources that entitle them to respectful consideration. Thus Van Buren and Keyes (*Genito-Urinary Diseases with Syphilis*, p. 380), state that it will sometimes happen—

"that patients with visceral syphilis, under protracted treatment, by large doses of iodide of potassium, will gradually show morning nausea, and upon examination their urine will be found light, slightly albuminous, and containing pale casts. In such cases the kidney-trouble is probably due to the irritation produced by the large amount of iodide of potassium passing through them, and the albumen and casts may be made to disappear, together with the morning nausea, by reducing the activity of the treatment. Several such cases have fallen under the author's observation."

In another place Keyes again writes (*Venereal Diseases*, 1880, p. 220): "I am certain that in some cases, slight, transient, albuminuria is produced by the prolonged use of the iodide of potassium in large doses." Mr. Jonathan Hutchinson in his famous address on syphilis before the Pathological Society of London (*Lancet*, 1, 1876, p. 204), thought that iodide of potassium, long-continued, might have had something to do with producing the long-continued albuminuria that preceded death in two cases of inherited syphilis in adults under his care. H. C. Wood (*Therapeutics, etc.*, p. 379), says: "During its passage through the kidneys, iodine undoubtedly exerts an influence upon these organs, as is shown by its producing albuminuria at times. It is indeed asserted, that it occasionally causes a true tubular nephritis." Statements such as these may be found in medical literature, but they lack definiteness, and can hardly be accepted as decisive. They must be received with a great deal of reserve, especially when we consider that the very extensive literature that has been devoted to the pathological effects of iodine and the iodides upon the system, is singularly meagre in references to these actions upon the kidneys, while the diuretic action of these drugs is universally recognized, and abundant proof of the morbific action often exerted by them upon different organs and tissues is everywhere available.

It is remarkable that alterations of the kidneys have been but rarely observed as resulting from their ingestion. Rodet, writing in 1847, states

that the ingestion of the iodide of potassium may induce nephritis, and records a case where the patient, 56 years old, took, for non-syphilitic disease, one gramme of the iodide daily for fifteen days, abundant hæmaturia resulting. This subsided after the medicine was discontinued, but recurred when it was again administered (*Gaz. Méd. de Paris*, 1847, p. 904). A very remarkable statement of Simon and Regnard may be found in *L'Union Médicale* (vol. 22, 1876, p. 26). It was noticed that two children (girls), to whose integument tincture of iodine had been applied over a limited surface, for different affections, betrayed some symptoms of iodism, along with a notable quantity of iodine in the urine, and albuminuria. Attention having been drawn to this fact, eleven children were submitted to the same treatment. Of these, four developed albuminuria. In three other cases, where the urine previous to the experiment contained neither iodine nor albumen, both became very evident after three days, soon ceasing to appear, but both reappearing upon the renewal of the application. Badin (*Thèse de Paris*, 1876), contributes in support of these observations two cases. The first patient, a phthisical girl nine years old, had tincture of iodine applied in front of and behind the chest. Albumen was detected in the urine after the third application, and disappeared after the iodine was abandoned. The second observation concerned a scrofulous girl, to whose skin tincture of iodine was applied. After the fourth application, the urine, which had been daily tested, became albuminous, regaining a healthy condition shortly after the conclusion of the experiment. Badin holds that this action is confined to children, the immunity of adults being complete ; and that it results from the passage of metallic iodine through the kidneys. These very interesting observations have never been confirmed, and, indeed, do not seem to have met with the attention they deserve. Should their correctness be established, it would still remain undecided how the albuminuria is produced ; whether, as claimed, by the action of free iodine upon the kidneys, or, as is not impossible, as the result of the simple covering of a considerable surface with an impermeable coating, such as has been known to produce similar effects under the use of a variety of substances.

A diligent search through a very extensive literature has afforded me only these scanty proofs of the irritating influence of iodine and the iodide upon the kidneys. On the other hand, while the almost entire absence of references to this subject in the very extensive discussions of the phenomena of iodism, during the last forty years, is, to say the least, very suggestive, we have the distinct statements of several writers, that renal affections are not induced by the iodides. This was the experience of Ricord (*Bulletin de Thérapeutique*, 1842, p. 164), and other writers. Arneth, Pelikan, and Zdekauer never found in the bodies of animals treated with iodine the smallest trace of renal disease (*Med. Zeitschr. Russlands*, 1856).

It is certainly important that we should have definite knowledge concerning the extent to which the presence of these agents in the system is capable of exciting structural alterations in the organs and tissues, and that in our treatment we should not expose our patients to unjustifiable risks. If, however, it be necessary to expose them to these dangers, we should do so with a full consciousness of the same, and be prepared to obviate them as far as possible.

With a view to ascertain to some extent the general condition of the kidneys of persons who suffer from late syphilis, as well as to note the effects of anti-syphilitic treatment upon these organs, I have made a series of observations of cases that have come under treatment, for the most part, in my out-patient service, but also to some extent in the wards of the University Hospital and Bayview Asylum (the city almshouse). They do not represent selected cases, but comprise all that were available during the period of my investigations, suffering from late syphilis, and who, with very few exceptions, had been more than three years syphilitic. My notes embrace memoranda of seventy patients, of whom, those whose condensed histories are subjoined, presented evidence of renal alterations.

Case 1.—Maria H., 32 years old, syphilitic for eight or nine years. Prostitute. Symptoms severe from the first. Much scarring. Present lesions ulcerative and extensive. General health much reduced. No dropsy. *Dec.* 29. Urine acid, sp. gr. 1022. Albuminous. Iodine reaction. Microscope reveals pus cells in abundance, but no tube casts. *Jan.* 24. Urine acid, sp. gr. 1017. Iodide reaction. Albuminuria. Microscope reveals a few hyaline and pale granular casts of the renal tubules. Pus cells and vaginal epithelium abundant. Has taken much iodide of potassium within the past year.

Case 2.—John P., 30 years old. Peddler. Syphilitic for thirteen years. Paraplegia five years ago. Epilepsy for two years. Great mental hebetude. Cranial nodes. Excruciating headache. *Jan.* 24, 1878. Has been taking iodide of potassium for some time. Has had no ulcerative lesion. Never had dropsy, but six years ago had some swelling of the feet. Heart healthy. Urine pale and with iodine reaction. Small amount of albumen. Some hyaline tube casts, here and there studded with a cell of renal epithelium. *April* 8. Urine neutral; pale; sp. gr. 1016. A slight cloudiness to nitric acid and heat. No tube casts. *May* 17. Urine acid and high coloured; sp. gr. 1030. Iodine reaction. Albumen copiously present. *Jan.* 14, 1879. Urine alkaline, pale, without iodine reaction. Very slight amount of albumen. No tube casts. *April* 11. Has taken no iodide since last entry. Urine acid, and freely albuminous. Uric acid crystals. Hyaline tube casts, some of them studded with renal epithelium.

Case 3.—Francis B., negro, 54 years old. Syphilitic more than twenty years. Has never had dropsy. Has led a hard life as a sailor on bay craft. Has now a gummatous ulcer of the penis. General health excellent. Heart normal. *Jan.* 15, 1878. Has had no treatment recently. Urine acid, and of sp. gr. 1026. Very slight precipitate to heat and nitric acid. Hyaline, pale, and coarsely-granular tube casts with renal epithelium. *Feb.* 23. Urine pale, acid, and of sp. gr. 1009. No

albumen. No iodine reaction. No tube casts. *March* 22. Has taken iodide of potassium for several weeks until the past few days. To-day the urine contains no iodine, but has a small amount of albumen, also a few pale granular tube casts. *April* 27. Has not been taking iodide. Urine dark, sp. gr. 1020. No iodine reaction. No albumen, a few very pale hyaline tube casts. *April* 17, 1879. No treatment since last entry. Urine free from albumen and tube casts.

Case 4.—Kate G., mulatto, 36 years old. Married. Syphilitic eight years. Very severe symptoms. Tubercular eruptions, ulcers, and gummy tumours of integument. Tibial and frontal nodes. Has taken much mercury and iodide of potassium. *Feb.* 4, 1878. Urine straw-coloured and acid; sp. gr. 1032. Iodine reaction. (Has been taking iodide since yesterday morning.) Slight albuminuria. Oxalate of lime crystals abundantly present. A few large and small hyaline tube-casts. *March* 6. Has taken no iodide for two weeks, until yesterday morning. Urine pale, acid; sp. gr. 1027. Iodine reaction. No albumen. Plenty of oxalate of lime, but no tube-casts. 14*th.* Has taken iodide regularly. Urine, acid; sp. gr. 1030. Iodine reaction. No albumen. No tube-casts. Oxalate of lime in abundance. *April* 8. Urine pale, alkaline; sp. gr. 1020. Small amount of albumen. *June* 3. Has taken no iodide for a month. Urine, acid and without iodine reaction. Small amount of albumen. Hyaline and granular casts. Oxalate of lime crystals. *Oct.* 24. Has been taking no iodide for some time. Urine faintly acid. No iodide reaction. No albumen. No tube-casts. Octohedra of oxalate of lime. *Nov.* 26. Gums slightly affected from biniodide of mercury, of which she has been taking $\frac{1}{12}$ gr. thrice daily, with her iodide. Urine gives iodine reaction; acid; no albumen. No tube-casts. *Dec.* 10. Has taken no iodide for four days. Urine free from iodine; acid; sp. gr. 1030. *March* 16, 1879. Has now been taking for several weeks 10 grains of iodide of potassium thrice daily. Urine shows no albumen to tests, but upon careful microscopic examination a few hyaline casts are detected. *April* 7. Has been taking iodine steadily. Urine, pale, acid; sp. gr. 1027. Iodine reaction. No albumen. Oxalate of lime and a few *mucous* tube-casts are discovered. *May* 15. Continues to take iodide as before. No albumen. No tube-casts. Oxalate of lime plentiful. *Feb.* 23, 1880. Has taken no iodide for some time. Urine normal. This patient has had upon one or two occasions slight swelling of the feet, but never decided dropsy.

Case 5.—Mrs. O., coloured, widow, 59 years old. Has had syphilis for 14 years. Faucial ulcers. Destruction of bony and soft parts of nose (partial). *Feb.* 17. Has been taking iodide of potassium for several weeks. Urine acid; sp. gr. 1017. Iodine reaction. Small amount of albumen. Hyaline and pale granular tube casts, the former numerous. *March* 1. Urine normal. 10*th.* Has taken no iodide since last entry. Urine pale and acid; sp. gr. 1013. No iodine reaction. Minute amount of albumen. Microscopically, uric acid crystals, many *mucous* tube-casts and a few hyaline casts. *April* 6. Urine faintly acid; sp. gr. 1013. (Has taken no iodide since last date.) No albumen. A few hyaline casts. *July* 1. Has taken no iodide since last date. Urine pale and acid; sp. gr. 1012. No iodine reaction. No albumen. No tube-casts. *Oct.* 22. Has not been taking iodide. Urine healthy. *Dec.* 12. Has taken no iodide since last date. Urine normal. *July* 9, 1879. Began to take iodide three days ago. Urine pale and faintly acid. Iodine reaction. No

albumen. A few *mucous* tube-casts. 25*th*. Urine pale. Iodine reaction exceedingly feeble. No albumen. Triple phosphates in abundance. Swarms of vibrios. After diligent search, a single hyaline cast is discovered. *Oct.* 1. Has taken no physic for some time. Urine normal. *March* 1, 1880. No physic. Urine healthy.

Case 6.—Sarah W., coloured; syphilitic for five years. Has had various systemic manifestations. Much "rheumatism." Has now phthisis pulmonalis. Has been taking mercury, iodide of potassium, and cod-liver oil. *March* 6, 1878. Urine shows presence of iodine; sp. gr. 1013. Albuminuria. Hyaline and granular tube-casts. *April* 17. Urine pale and acid; sp. gr. 1010. No iodine reaction. Albumen present in large quantity. Pale and coarsely granular tube casts. This woman had a large cavity in the apex of her right lung, and had been anasarcous.

Case 7.—M. G., white, about 50 years old. Twenty years syphilitic. During this period has suffered from many forms of constitutional manifestations. Has been hemiplegic for several years. Last summer she took thirty-grain doses of iodide of potassium thrice daily. Is not at present under treatment. *March* 6, 1878. Urine very pale, alkaline; sp. gr. 1010. No iodine reaction. Albuminuria. *April* 17. Urine pale, faintly acid; sp. gr. 1006. No iodine reaction. Small amount of albumen. Hyaline and pale granular casts present.

Case 8.—Kate M., negress, aged 46 years. Syphilitic nearly twenty-four years. Has had various eruptions and very much "rheumatism." Much headache, nausea, and vomiting. Has had dropsy. Heart normal. She is very obese. Has been taking iodide of potassium for twenty-five months. Now takes ten grains thrice daily. *April* 2, 1878. Urine pale; sp. gr. 1023. No iodine reaction (!). No albumen. Lozenge crystals of uric acid, and *mucous* tube casts. Likewise a number of hyaline and pale granular tube casts. 17*th*. Urine, acid; sp. gr. 1022. Iodine reaction. A barely perceptible amount of albumen is present. Uric acid crystals and hyaline and pale granular casts.

Case 9.—Lottie L., coloured, 29 years old. Syphilitic for several years. Cachectic. Broad condylomata of perineum. Also of vulval and anal regions. Enormous hypertrophy of left labium majus and clitoris, equalling a cocoanut in size. Has been taking iodide of potassium for some time. At present has twenty grains thrice daily. *March* 31. Urine acid; sp. gr. 1011. Considerable pus present. Albumen in limited amount. Iodine reaction. Hyaline tube casts. Nausea and dyspepsia trouble her greatly. Has never had dropsy. Heart healthy.

Case 10.—Annie B., 25 years old. Syphilitic ten years. Various constitutional manifestations, and extensive ulcerations. Several years since, her left leg was amputated, in consequence of intractable ulceration and necrosis. Has had much iodide of potassium, and is now taking 20 grains thrice daily. *April* 2. Urine straw-coloured, acid; sp. gr. 1016. Iodine reaction. Copious amount of albumen. Multitudes of hyaline, pale, and coarsely granular tube-casts, some studded with renal epithelium and blood disks, some fatty. 17*th*. Urine acid; sp. gr. 1012. No iodine reaction. Highly albuminous. She has at several times been anasarcous, not so at present. Heart hypertrophied; valves normal. Casts not coloured by solution of iodine.

Case 11.—John P., 21 years old, sailor. Syphilitic since 1872. Sore throat; iritis; "rheumatism;" periostitis. Has had various skin manifestations. Has taken iodide of potassium for seven weeks, never before.

May 1, 1878. Urine high-coloured, acid; sp. gr. 1023. Iodine reaction. No precipitate to heat and nitric acid. No tube-casts present, but large numbers of oxalate of lime octohedra. 28*th*. Urine acid; sp. gr. 1030. Iodine reaction. Oxalate of lime octohedra of very minute size. A goodly number of mucous casts, and a few well-defined hyaline tube-casts. *June* 10. Urine acid; sp. gr. 1027. Iodine reaction. No albumen. Careful search through several slides reveals, in addition to oxalate of lime, octohedra and mucous casts, a single hyaline tube-cast. 16*th*. Urine acid. Iodine reaction. No albumen. Mucous tube-casts. No crystalline deposit. No hyaline casts. This patient had no history of dropsy. His heart was healthy.

Case 12.—B. F. T., coloured, sailor, 25 years old. Syphilitic for four years. Frequent and various cutaneous eruptions. Iritis. Has had suppurative adenitis. Has been taking iodide of potassium for one year; now takes 10 grains thrice daily. *May* 18. Urine acid; sp. gr. 1020. Iodine reaction. No albumen. Microscopically, a few pus-cells and hyaline tube-casts, also a few pale granular casts. 26*th*. Urine acid; sp. gr. 1023. Iodine reaction. No albumen. Hyaline and pale granular tube-casts. *June* 1. Urine acid; sp. gr. 1030. Iodine reaction. No albumen. The microscope reveals only a few oxalate of lime octohedra. 16*th*. Has taken no iodide for several days. No iodine reaction. No albumen. No tube casts. Octohedra of oxalate of lime. 25*th*. Urine acid. No iodine reaction. No tube-casts. Oxalate of lime crystals. *July* 2. Has been taking iodide of potassium for one week. Acid urine; sp. gr. 1028. No albumen. Microscopically, a few oxalate of lime octohedra and many hyaline and granular tube-casts. (No history of dropsy.)

Case 13.—J. M., white, sailor, 30 years old. Initial lesion twelve years ago. Various cutaneous affections. "Rheumatism." Iritis. Has been taking 10 grains of iodide of potassium thrice daily for five months. *May* 18, 1878. Pale and acid urine; sp. gr. 1017. Iodine reaction. No albumen. Some hyaline tube-casts are visible. 28*th*. Urine acid; sp. gr. 1022. No abnormal deposit. *June* 1. Urine acid; sp. gr. 1022. No albumen. No iodine reaction. No abnormal microscopic condition. *June* 16. Urine acid. Iodine reaction. No albumen. A number of sharply defined hyaline tube-casts. (He had not been taking iodide for nearly a month, but upon a recurrence of iritis, its use was resumed several days ago.) 25*th*. Urine acid. No albumen. Iodine reaction. Well defined and perfectly hyaline tube-casts.

Case 14.—S. J., negro, 23 years old. Initial lesion in March, 1873. Copious general eruptions, alopecia, ulcerative lesions, pulmonary hemorrhages, dulness over right apex in front and behind. (Oct. 1877.) *June* 13, 1878. Pulmonary softening and cavities. Very pronounced general adenopathy. Urine pale, alkaline; sp. gr. 1020. No iodine reaction. Large amount of albumen. Microscopically, triple phosphates, but no tube-casts. 15*th*. Urine pale, alkaline. Albumen present in smaller amount. Many pus-corpuscles. No tube-casts.

Case 15.—J. B., sailor, 32 years old. Initial lesion during the spring of 1872. Has now (July 14, 1879), ulcers upon legs, and many scars upon back, breast, and legs. The entire back is covered with scar-tissue forming an immense surface of cicatricial bands and depressions, the colour of which still shows the dusky red of recent repair. He took some iodide of potassium in 1874. Takes at present 4 grains, with $\frac{1}{16}$ gr. of bin-iodide of mercury thrice daily. Urine acid; sp. gr. 1020. Iodine reac-

tion. No albumen. Associated with minute oxalate of lime octohedra and pus-cells, there are quite a number of casts of the tubules, some mucous, others ordinary pale granular casts, which are very numerous. *July* 29. Has taken no iodide for two weeks. Urine acid; sp. gr. 1022. No albumen. No iodine reaction. No tube-casts. Some oxalate of lime octohedra. *Aug.* 6. Urine acid; sp. gr. 1008. No iodine reaction. No abnormal deposit. No albumen.

Case 16.—F. J. K., 45 years old, paperhanger. Initial lesion twenty-five years ago. Symptoms of varied character since that time. Has now deep ulceration on breast and abdomen. Some œdema of lower extremities. Line of hepatic dulness reaches below the level of the umbilicus, but recedes rapidly towards the left. Patient very thin and sallow, but not distinctly jaundiced. Some ascites. Girth at umbilical level 84 cm. General health much reduced. Has had paralysis of eye muscles. Can give no account of treatment, except of a profuse salivation. Takes now 8 grains of iodide of potassium thrice daily. *July* 21, 1879. Urine acid; sp. gr. 1006. Iodine reaction. Small quantity of albumen. No tube-casts. 23*d*. Urine pale and acid; sp. gr. 1010. Copious precipitate of albumen, and, microscopically, abundant tube-casts, granular and epithelial. Iodine reaction. *Aug.* 5. Urine acid; sp. gr. 1008. Iodine present. Much albumen. Hyaline tube-casts in small numbers. *Sept.* 9. General condition much improved. Ulcers healed. Urine albuminous and with hyaline and granular tube-casts. Heart enlarged, but valves healthy.

Case 17.—H., sailor, 30 years old. Chancre five years ago. Various constitutional symptoms, but no ulceration. Right hemiplegia and aphasia for two months. Improvement under the iodide of potassium. *Aug.* 6. Urine not albuminous; acid; sp. gr. 1022. Copious deposit of oxalate of lime octohedra, and many hyaline tube-casts. 9*th*. Urine pale. Not albuminous. Iodine reaction. No tube-casts. Has not been taking iodide for several days. *Sept.* 5. Iodide resumed. Urine shows iodine reaction; acid. Mucous and hyaline tube-casts and oxalate of lime octohedra in small numbers. 23*d*. Urine acid; sp. gr. 1010. Iodine reaction. No albumen. No tube-casts. *Oct.* 22. Urine free from albumen and tube-casts, but with oxalate of lime in small quantity. Heart normal. No dropsy.

Case 18.—An elderly sailor, wretchedly emaciated and with pronounced cachexia, just from shipboard. Unable to stand. Can give no history. Body is seamed with white flat scars. Breath disgustingly fetid from deep faucial and pharyngeal ulceration. Large nodes upon right radius and ulna. No dropsy. Vomiting incessantly for several days. Death in three days apparently of exhaustion, without paralysis and with intellect clear to the last. Urine, examined day of admission (Aug. 13), was acid, of sp. gr. 1014. Small amount of albumen. Plenty of tube-casts, mucous, hyaline, and granular. *Post-mortem examination:* Kidneys dark brown. Capsules moderately adherent. Left kidney much smaller than right. Both hard and contracted, but without circumscribed alterations. No signs of gummy infiltration in any part of abdominal cavity. Upon the spleen, which was slightly enlarged, there was a flattened, whitish mass of cartilaginous hardness, lozenge-shaped and measuring 3×2cm.

Case 19.—B. R. Ostler; Irish; married. Chancre in Jan. 1876, followed by severe constitutional symptoms. *Oct.* 15, 1879. Deep ulceration of right leg. Left testicle as large as a hen's egg, smooth, evenly enlarged, and painless. Patient is a large, burly man of dissipated habits.

Urine acid; sp. gr. 1020. No albumen, but numerous hyaline and granular casts of the tubules. Begins to take iodide of potassium in 5 gr. doses thrice daily. *Dec.* 13. Urine free from albumen and tube-casts. Abundant uric acid crystals and oxalate of lime. 22*d*. Still takes iodide. Urine not albuminous. Copious deposit of amorphous urates and a few hyaline and granular casts.

Thus, it will be observed that of 70 cases investigated by me, 19 betrayed evidences of renal disturbance; 13 being characterized by the presence of albumen in the urine, constantly or at irregular intervals, while in 18 the microscope revealed, in the urine, casts of the renal tubules. In 12 cases albumen and tube-casts were simultaneously present. It is at once manifest that the kidneys were affected in very different degrees in the different cases. In few instances were the evidences of kidney disease pronounced and constant. For the most part, they were slight and transitory, and my observations are remarkable rather for the large proportion where renal disturbances were detected, than for their gravity. For the present, I propose to turn aside from many of the interesting features of these cases, and to ask attention to the influence that may possibly have been exerted by the iodide of potassium in the production of abnormal conditions. For the purposes of such an investigation, a certain number of my cases may be excluded, as offering examples of pronounced renal degeneration, the exciting cause of which was buried in obscurity, and others, where the changes, though slight, existed already when first coming under notice, and before the iodide of potassium was administered. Similarly, must be excluded those cases where the albumen or tube-casts, or both, though irregularly and transitorily present in the urine and perhaps in some instances dependent upon the iodide of potassium, could not with any show of probability be traced to the ingestion of this drug.

Before proceeding to consider the cases where iodide of potassium did seem to exert an influence in exciting the morbid symptoms, let me briefly call attention to the very large proportion of cases where oxalate of lime crystals will be found in the urine of persons taking the iodide. Thus, of a series of observations of 81 cases, oxalate of lime crystals (usually in abundance, sometimes scantily) were detected in 21 cases. The urine of these 21 patients contained lime oxalate octohedra 39 times; and in 29 of these observations the simultaneous presence of iodine was ascertained. Although we may no longer accept the views of Golding-Bird and Prout concerning an oxalic acid diathesis or oxaluria, but must consider the condition simply as a manifestation of lithiasis, a result of imperfect oxidation, we may still in the present instance fairly assume that this incomplete oxidation is in some manner the result of the influence of the iodide of potassium in disturbing the digestive processes, or otherwise interfering with normal nutrition and metamorphosis.

The cases coming under my observation, where inconsiderable disturb-

ance of the renal organs was associated with the administration of the iodide of potassium, have been, as I have shown, proportionally numerous. In only a few was it possible to attribute to the drug, with any degree of confidence, a causative influence in exciting the derangement. Simply asking attention, therefore, to the frequent association of evidences of renal irritation with the presence of the iodide of potassium in the circulation, I pass to the consideration of those cases where the iodide of potassium seemed to determine the abnormal condition of the kidneys. Case 5, for example, had been taking the drug for some weeks previous to my first observation, when albumen in small amount and hyaline and granular tube-casts were discovered. Shortly after the medicine was discontinued, the albumen disappeared from the urine, but it was not until the expiration of four months that the urine became perfectly normal, so far as concerns the presence of tube-casts, as shown by several examinations extending over a period of six months. My patient was not again seen for an additional six months, when the urine, examined three days after resuming the use of the iodide, revealed only mucous casts. Three weeks subsequently, diligent search revealed a single hyaline cast. Treatment was again suspended, and at the expiration of two months the urine was normal, as far as concerns albumen and tube-casts; and so it remained at the end of another six months. Case 12 likewise justifies to a great extent the suspicion that renal irritation, resulting in the formation of tube-casts, followed the ingestion of the iodide. This patient had been taking the remedy nearly one year. Albumen was not detected in the urine, but a number of hyaline and pale granular casts were discovered. A week later a similar condition was ascertained. Four days later the urine appeared normal, the ingestion of the iodide having been discontinued. The medicine was not renewed for a month, during which time the urine was twice examined and found healthy. A week after the treatment was recommenced, many hyaline and pale granular casts of the renal tubules were detected, but no albumen. Case 13 presents features showing the same tendency. The patient, a sailor 30 years old, had been twelve years syphilitic. He had been taking iodide of potassium in ten-grain doses, thrice daily, for five months. His urine, examined May 18, was acid, of sp. gr. 1017, and contained iodine. There was no albumen, but hyaline casts were present. *May* 28. Urine healthy. *June* 1. Urine without iodine, albumen, or tube-casts. *June* 16. (He had not been taking iodide since the middle of May, but upon the supervention of a new attack of iritis it was resumed several days previous to this date.) The urine was without albumen, but contained iodine and a goodly number of well-defined hyaline tube-casts. *June* 25. Urine acid. No albumen. Iodine reaction. Well defined hyaline tube-casts. Case 15 also seemed to exhibit renal irritation from the ingestion of iodide of potassium. He had late syphilis and was taking four grains of iodide of potassium thrice daily. His urine con-

tained hyaline and granular tube-casts, but no albumen. His iodide was stopped for three weeks. His urine, examined at the end of this period, showed no iodine reaction, no albumen, and, microscopically, no tube-casts. Examined again after a week, it remained free from abnormal appearances.

The following cases, abstracted from my note-book, though not included in the regular series of observations, on account of the recent date of the acquirement of syphilis, and not occurring in order, are of especial interest, as bearing upon the point under discussion :—

Case 20.—S. F. B., a young negro, hostler, had a chancre of the penis about Christmas, 1877. April 6, 1878, he had a copious pustular syphiloderm, and complained of very extensive "rheumatism." For this he had been taking, for a few days, the iodide of potassium. His urine, examined on the above date, was acid, of sp. gr. 1022, and showed the presence of iodine to the test. There was no deposit to heat and nitric acid; no tube-casts. The treatment was continued more or less regularly until June 6, when the urine was straw-coloured and acid. The presence of iodine was ascertained; there was no albumen; crystals of uric acid and oxalate of lime were detected, and with them well-marked hyaline tube-casts. He now ceased to take the iodide, and his urine, at the end of two weeks, contained neither albumen nor tube-casts. The iodide was not resumed, and the urine examined July 9, 1878, Jan. 7 and 15, 1879, remained perfectly healthy.

Case 21.—James W., Irish, 32 years old. Had a chancre during the latter part of Sept. 1877, followed by extensive papular syphiloderm. His urine, examined Jan. 15, 1878, was pale, of acid reaction, and of sp. gr. 1022. Albumen was not present, and the microscope revealed no signs of renal disease. Nodes beginning to appear on the tibia, accompanied by excruciating nocturnal pains in the knees, the iodide of potassium was now ordered, and was continued irregularly until March 28, with, for short intervals, a small amount of mercury. At the latter date his urine was pale, faintly acid, of sp. gr. 1028, and was free from albumen. There was a slight sediment of oxalate of lime octohedra, and some mucous tube-casts. The iodide was continued until early in May. The urine examined May 20 was without iodine reaction, but contained a small amount of albumen and numerous hyaline and pale granular tube-casts. The patient remained irregularly under treatment for some months longer, and then was not again seen until Sept. 4, 1879, when he had taken no medicine for a considerable time. His urine was free from albumen and tube-casts.

Although, in the greater number of my cases, no definite connection between the iodide ingested and the albumen or tube-casts found in the urine could be established, the occurrence of the latter was unexpectedly frequent, and out of all proportion to what is usually supposed to prevail. It is true that the number where pronounced renal disease was present was probably not much larger than will often be found in the wards and out-patient departments of large city hospitals. The point to which I especially desire to call attention is, that in so many of my patients albumen or tube-casts, or both, were detected, chiefly, however, as transitory phenomena,

the former in minute quantity, the latter in the forms indicative of the smallest amount of renal alteration.

The question arises here, very naturally, of the significance of the presence of albumen in small quantity and of hyaline casts of the renal tubules in the urine. So far as concerns the albumen there seems to be no reason to believe that it is present in healthy urine, or to doubt that the presence in the urine of even a small amount indicates a departure from health. "We must admit, however, that it may make its appearance under such conditions as to show only a very slight deviation from the natural state." (Ellis, *Boston Med. and Surg. Journ.*, vol. cii., 1880, p. 361.) So far, then, as albumen was present in the urine of these patients, we may conclude that it was as a result of pathological processes. In quite a number of the cases, however, hyaline and pale granular tube-casts were the sole evidences of a morbid condition of the kidneys. I have already referred to the unusual frequency of oxalate of lime-crystals, and their probable dependence upon the ingestion of the iodide of potassium. Should the same influence determine the appearance of the tube-casts, to what extent may these be considered to be the results of tissue change? In other words, may hyaline casts of the renal tubules be found in the urine of persons whose kidneys are healthy?

It has not unfrequently been asserted that hyaline tube-casts may appear in urine from healthy kidneys. Henle, for example, claimed to have frequently discovered them in healthy kidneys. (*Handbuch der Systemat. Anat. der Mench.*) Charcot also states that they may appear in the urine when the kidneys are not diseased, and says that the same assertion has been made by Robin, Axel Key, and others (Tyson, *Phila. Med. Times*, vol. x. p. 293). Nearly all authorities, however, consider the presence of tube-casts, of any variety (except, possibly, the mucous), as indicative of morbid change in the kidneys. Bartels declares (*Ziemssen's Cyclopædia*, vol. xv.) that true casts are never found under normal conditions, and that as a general rule they are attended with the excretion of albumen (p. 87). It seems to be pretty certain that hyaline casts of the renal tubules are the results of irritation of the epithelia of these tubules, in consequence of which a coagulable material is secreted by these cells, which coalesces into cylinders, corresponding to the shapes of the tubules. (*Aufrecht. Centrabl. f. d. Med. Wissensch.*, 19, 1878; Langhaus, *Virchow's Archiv*, lxxvi. 85, Oedmanson, Rovida, and others.)

To what extent these casts may be evidences of tissue alterations it is impossible to say. It is certainly reasonable to suppose that at least they may be results of transient irritation that may subside without leaving its vestiges behind in the tissues of the organs. There can be no doubt that patients suffering from acute febrile disease may, during life, pass urine containing both albumen and tube-casts, and yet the kidneys of these persons may reveal nothing abnormal after death. This would simply

indicate that the irritation that was sufficient to stimulate the glandular epithelium to the formation of casts, was not violent enough or sufficiently long continued to produce recognizable structural alterations. It must, therefore, be understood, that the influences producing these casts may vary from a slight stimulation of the epithelia of the tubules to extensive and irreparable destruction of renal substance; but it must not be forgotten that while an insignificant and transient irritation may subside without leaving its traces behind it, it is most probable that if it be continued for an indefinite time it may finally produce permanent effects. In the cases I have recorded, the results from the irritation of the iodide were, as observed, at most slight albuminuria and pale granular tube-casts. Nor was there noticed, in any of them, systemic evidences of renal disturbance. Certainly in no case was there the slightest reason to suspect, as produced by the iodide, an extensive parenchymatous inflammation, such as it has been claimed the iodide is capable of exciting. The effects were such as iodine and the iodides may occasion in mucous membranes generally, a catarrh, in fact. Beyond this it did not proceed, but, on the other hand, there seemed rather to be a tendency towards a subsidence of the irritation and a toleration of the drug. At least, there seemed to be no increase in the symptoms under its use, and in one case especially, that of K. G. (Case 4), the renal affection that had been quite pronounced, gradually and completely disappeared under the full and systematic use of the iodide. It is not impossible, however, that in this instance the results were due to the specific action of the drug upon a purely syphilitic renal disorder.

At the same time, I cannot avoid the conclusion that while the evil effects of the iodide of potassium upon the kidneys are small and for the most part transitory, the occurrence of more severe alterations is not impossible, nay, is probable. But upon this point my investigations have been too few and imperfect to enable me to speak with confidence. It is perfectly well established that there is no constant tendency on the part of the kidneys to resent the presence of the iodide. My own observations are confirmatory of this, for they include a number of old syphilitics, to whom the drug had been administered for protracted periods, and in excessive doses, without the smallest sign of urinary disorder. As in other parts of the body, the undesirable effects of the ingestion of iodine and the iodides have been attributed to idiosnycrasy, so must idiosnycrasy be invoked to explain any undesirable results of the action of these preparations upon the kidneys.

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